Journal of

MEDICAL GENETICS

VOLUME 37 · 2000

Editor: Eamonn R Maher
Associate Editors: Charis Eng
Willie Reardon
Guy Van Camp
Technical Editor: Clare Henderson
Editorial Assistant: Anita Starbuck

EDITORIAL COMMITTEE

L Aaltonen (Finland)
S E Antonarakis (Switzerland)
J Burn (UK)
H Brunner (The Netherlands)
D F Callen (Australia)
G Evers-Kiebooms (Belgium)
R J M Gardner (Australia)
R J Gorlin (USA)
A G Knudson Jr (USA)
C Larsson (Sweden)
E Legius (Belgium)
D Malkin (Canada)
A Munnich (France)
B Ponder (UK)
K A Schneider (USA)
T Strachan (UK)
R Trembath (UK)
H Torriello (USA)
M Warman (USA)
M Zeviani (Italy)
Editor,
British Medical Journal

APPOINTED BY THE BRITISH MEDICAL ASSOCIATION

BRITISH MEDICAL ASSOCIATION · TAVISTOCK SQUARE · LONDON WC1H 9JR

VOLUME 37 · CONTENTS

No 1 JANUARY 2000

Page

Review articles

1 Friedreich ataxia: an overview *M B Delatycki, R Williamson, S M Forrest*

9 The molecular genetics of Marfan syndrome and related microfibrillopathies *P N Robinson, M Godfrey*

Original articles

26 Evidence for digenic inheritance in some cases of Antley-Bixler syndrome? *W Reardon, A Smith, J W Honour, P Hindmarsh, D Das, G Rumsby, I Nelson, S Malcolm, L Adès, D Sillence, D Kumar, C DeLozier-Blanchet, S McKee, T Kelly, W L McKeehan, M Baraitser, R M Winter*

33 An HDR (hypoparathyroidism, deafness, renal dysplasia) syndrome locus maps distal to the DiGeorge syndrome region on 10p13/14 *P Lichtner, R König, T Hasegawa, H van Esch, T Meitinger, S Schuffenhauer*

38 Prevalence of mitochondrial gene mutations among hearing impaired patients *S-I Usami, S Abe, J Akita, A Namba, H Shinkawa, M Ishii, S Iwasaki, T Hoshino, J Ito, K Doi, T Kubo, T Nakagawa, S Komiyama, T Tono, S Komune*

41 Prevalent connexin 26 gene (*GJB2*) mutations in Japanese *S Abe, S-I Usami, H Shinkawa, P M Kelley, W J Kimberling*

44 A search for evidence of somatic mutations in the *NF1* gene *A M John, M Ruggieri, R Ferner, M Upadhyaya*

Short reports

50 A connexin 26 mutation causes a syndrome of sensorineural hearing loss and palmoplantar hyperkeratosis (MIM 148350) *K Heathcote, P Syrris, N D Carter, M A Patton*

52 Exclusion of chromosome 9 helps to identify mild variants of acromesomelic dysplasia Maroteaux type *L Faivre, M le Merrer, A Megarbane, B Gilbert, G Mortier, V Cusin, A Munnich, P Maroteaux, V Cormier-Daire*

55 Mutational analysis of the tuberous sclerosis gene *TSC2* in patients with pulmonary lymphangioleiomyomatosis *A Astrinidis, L Khare, T Carsillo, T Smolarek, K-S Au, H Northrup, E P Henske*

58 Cryptic subtelomeric translocations in the 22q13 deletion syndrome *V Praphanphoj, B K Goodman, G H Thomas, G V Raymond*

Letters to the Editor

62 Risk of multisystem disease in isolated ocular angioma (haemangioblastoma) *A R Webster, E R Maher, A C Bird, A T Moore*

63 Confirmation of the assignment of the Sanjad-Sakati (congenital hypoparathyroidism) syndrome (OMIM 241410) locus to chromosome lq42-43 *T E Kelly, S Blanton, R Saif, S A Sanjad, N A Sakati*

64 Molecular diagnosis is important to confirm suspected pseudoachondroplasia *B Newman, D Donnai, M D Briggs*

65 Biallelic expression of *IGFBP1* and *IGFBP3*, two candidate genes for the Silver-Russell syndrome *E L Wakeling, M P Hitchins, S N Abu-Amero, P Stanier, G E Moore, M A Preece*

67 Mutational analysis of the human pancreatic secretory trypsin inhibitor (*PSTI*) gene in hereditary and sporadic chronic pancreatitis *J-M Chen, B Mercier, M-P Audrezet, C Ferec*

70 A case of inv dup(8p) with early onset breast cancer *M Seltmann, P Harrington, B A J Ponder, L R Willatt, A C Heppell-Parton, H Anton-Culver*

71 Appendiceal carcinoma complicating adenomatous polyposis in a young woman with a de novo constitutional reciprocal translocation t(5;8)(q22;p23.1) *D Koorey, N J Basha, C Tomaras, J Freiman, L Robson, A Smith*

75 *NF2* gene deletion in a family with a mild phenotype *C López-Correa, J Zucman-Rossi, H Brems, G Thomas, E Legius*

77 Absence of fragile X syndrome in Nova Scotia *R G Beresford, C Tatlidil, D C Riddell, J P Welch, M D Ludman, P E Neumann, W L Greer*

80 **Notice for contributors**

No 2 FEBRUARY 2000

Page

Commentary

81 Of palms, soles, and gums *R J Gorlin*

Review article

83 Genetic susceptibility to age related macular degeneration *J R W Yates, A T Moore*

Original articles

88 Haim-Munk syndrome and Papillon-Lefèvre syndrome are allelic mutations in cathepsin C *T C Hart, P S Hart, M D Michalec, Y Zhang, E Firatli, T E Van Dyke, A Stabholz, A Zlotogorski, L Shapira, W A Soskolne*

95 Localisation of a gene for prepubertal periodontitis to chromosome 11q14 and identification of a cathepsin C gene mutation *T C Hart, P S Hart, M D Michalec, Y Zhang, M L Marazita, M Cooper, O M Yassin, M Nusier, S Walker*

102 Disruption of heart sarcoglycan complex and severe cardiomyopathy caused by β sarcoglycan mutations *R Barresi, C Di Blasi, T Negri, R Brugnoni, A Vitali, G Felisari, A Salandi, S Daniel, F Cornelio, L Morandi, M Mora*

108 Evaluation of a counselling protocol for predictive genetic testing for hereditary non-polyposis colorectal cancer *K Aktan-Collan, J-P Mecklin, A de la Chapelle, P Peltomäki, A Uutela, H Kääriäinen*

114 Identification of supernumerary marker chromosomes derived from chromosomes 5, 6, 19, and 20 using FISH *P Stankiewicz, E Bocian, K Jakubów-Durska, E Obersztyn, E Lato, H Starke, K Mroczek, T Mazurczak*

121 A supernumerary marker chromosome originating from two different regions of chromosome 18 *B Röthlisberger, K Chrzanowska, D Balmer, M Riegel, A Schinzel*

Short reports

125 5p14 deletion associated with microcephaly and seizures *E I Johnson, R C Marinescu, H H Punnett, B Tenenholz, J Overhauser*

128 A microdeletion in 19q13.2 associated with mental retardation, skeletal malformations, and Diamond-Blackfan anaemia suggests a novel contiguous gene syndrome *D Tentler, P Gustavsson, G Elinder, O Eklöf, L Gordon, A Mandel, N Dahl*

132 First description of germline mosaicism in familial hypertrophic cardiomyopathy *J-F Forissier, P Richard, S Briault, C Ledeuil, O Dubourg, B Charbonnier, L Carrier, C Moraine, G Bonne, M Komajda, K Schwartz, B Hainque*

Perspectives

135 Shared decision making and non-directiveness in genetic counselling *G Elwyn, J Gray, A Clarke*

Letters to the Editor

139 The CAG repeat within the androgen receptor gene in male breast cancer patients *I E Young, K M Kurian, M A F Mackenzie, I H Kunkler, B B Cohen, M L Hooper, A H Wyllie, C M Steel*

141 Deletion and duplication of the adenomatous polyposis coli gene resulting from an interchromosomal insertion involving 5(q22q23.3) in the father *R J Hastings, E C Svennevik, B Setterfield, D Wells, J D A Delhanty, H Mackinnon*

145 Hypoparathyroidism, retarded growth and development, and dysmorphism or Sanjad-Sakati syndrome: an Arab disease reminiscent of Kenny-Caffey syndrome *A S Teebi*

146 Tandem duplication with the neurofibromatosis type 1 gene (*NF1*) and reciprocal t(15;16)(q26.3;q12.1) translocation in familial association of NF1 with intestinal neuronal dysplasia type B(INDB) *M Bahuau, I Laurendeau, A Pelet, B Assouline, T Lamireau, L Taine, B Le Bail, P Vergnes, S Gallet, M Vidaud, S Lyonnet, D Lacombe, D Vidaud*

150 Identification of novel alleles at a polymorphic microsatellite repeat region in the human *NRAMP1* gene promoter: analysis of allele frequencies in primary biliary cirrhosis *A M Graham, M M Dollinger, S E M Howie, D J Harrison*

152 No evidence for imprinting in distal 18q *R Maiwald, J Overhauser, F Laccone*

156 Renal angiomyolipomata and learning difficulty in tuberous sclerosis complex *F J K O'Callaghan, M Noakes, J P Osborne*

157 Clinical geneticists' attitudes and practice towards testing for breast cancer susceptibility genes *A M Lucassen, R S Houlston*

No 3 MARCH 2000

Page

Review article

161 Detecting low penetrance genes in cancer: the way ahead *R S Houlston, I P M Tomlinson*

Original articles

168 Diagnostic analysis of the Rubinstein-Taybi syndrome: five cosmids should be used for microdeletion detection and low number of protein truncating mutations *F Petrij, H G Dauwerse, R I Blough, R H Giles, J J van der Smagt, R Wallerstein, P D Maaswinkel-Mooy, C D van Karnebeek, G-J B van Ommen, A van Haeringen, J H Rubinstein, H M Saal, R C M Hennekam, D J M Peters, M H Breuning*

177 Mutation analysis in glutaric aciduria type I *J Zschocke, E Quak, P Guldberg, G F Hoffmann*

182 Butyrylcholinesterase K variant is genetically associated with late onset Alzheimer's disease in Northern Ireland *S P McIlroy, V L S Crawford, K B Dynan, B M McGleenon, M D Vahidassr, J T Lawson, A P Passmore*

186 Age and sex based genetic locus heterogeneity in type 1 diabetes *A D Paterson, A Petronis*

192 A model protocol evaluating the introduction of genetic assessment for women with a family history of breast cancer *J Gray, K Brain, P Norman, C Anglim, E France, G Barton, L Branston, E Parsons, A Clarke, J Sampson, E Roberts, R Newcombe, D Cohen, C Rogers, R Mansel, P Harper*

197 Why do women attend familial breast cancer clinics? *K Brain, J Gray, P Norman, E Parsons, A Clarke, C Rogers, R Mansel, P Harper*

Clinical genetics in practice

203 Guidelines for a genetic risk based approach to advising women with a family history of breast cancer *D M Eccles, D G R Evans, J Mackay, on behalf of the UK Cancer Family Study Group (UKCFSG)*

Letters to the Editor

210 No evidence of germline *PTEN* mutations in familial prostate cancer *M S Forrest, S M Edwards, R A Hamoudi, D P Dearnaley, A Arden-Jones, A Dowe, A Murkin, J Kelly, M D Teare, D F Easton, M A Knowles, D T Bishop, R A Eeles*

212 Mutation analysis of *H19* and *NAP1L4* (*hNAP2*) candidate genes and *IGF2* DMR2 in Beckwith-Wiedemann syndrome *D Catchpoole, A V Smallwood, J A Joyce, A Murrell, W Lam, T Tang, D Munroe, W Reik, P N Schofield, E R Maher*

215 A novel mutation in the *CFTR* gene correlates with severe clinical phenotype in seven Hispanic patients *J Wang, M C Bowman, E Hsu, K Wertz, L-J C Wong*

219 The continuing failure to recognise Alström syndrome and further evidence of genetic homogeneity *V J Deeble, E Roberts, A Jackson, N Lench, G Karbani, C G Woods*

220 Clinical and radiographic features of a family with hypochondroplasia owing to a novel Asn540Ser mutation in the fibroblast growth factor receptor 3 gene *G Mortier, L Nuytinck, M Craen, J-P Renard, J G Leroy, A de Paepe*

224 Screening British CADASIL families for mutations in the *NOTCH3* gene *R P J De Lange, J Bolt, E Reid, R da Silva, D J Shaw, D M St Clair*

225 Correlation between mutations and age in cystic fibrosis in a French Canadian population *S R Rivard, C Allard, J-P Leblanc, M Milot, G Aubin, F Simard, C Férec, M de Braekeleer*

227 The heritability of high myopia: a reanalysis of Goldschmidt's data *J A Guggenheim, G Kirov, S A Hodson*

231 Progressive neurological deterioration in a child with distal arthrogryposis and whistling face *D Lev, M Yanoov, S Weintraub, T Lerman-Sagie*

233 Chromosomal duplication of band 10p14 segregating through four generations *L Voullaire, R J M Gardner, C Vaux, A Robertson, R Oertel, H Slater*
238 Somatic mosaicism associated with a mild Alport syndrome phenotype *K E Plant, E Boye, P M Green, D Vetrie, F A Flinter*
240 **Notice for contributors**

No 4 APRIL 2000

Page **Original articles**
241 A locus for primary ciliary dyskinesia maps to chromosome 19q *M Meeks, A Walne, S Spiden, H Simpson, H Mussaffi-Georgy, H D Hamam, E L Fehaid, M Cheehab, M Al-Dabbagh, S Polak-Charcon, H Blau, A O'Rawe, H M Mitchison, R M Gardiner, E Chung*
245 Localisation of the gene causing diaphyseal dysplasia Camurati-Engelmann to chromosome 19q13 *K Janssens, R Gershoni-Baruch, E Van Hul, R Brik, N Guañabens, N Migone, L A Verbruggen, S H Ralston, M Bonduelle, L Van Maldergem, F Vanhoenacker, W Van Hul*
250 Mutation screening in Rett syndrome patients *F Xiang, S Buervenich, P Nicolao, M E S Bailey, Z Zhang, M Anvret*
256 Genetic heterogeneity of Usher syndrome type II: localisation to chromosome 5q *S Pieke-Dahl, C G Möller, P M Kelley, L M Astuto, C W R J Cremers, M B Gorin, W J Kimberling*
263 Report of five novel and one recurrent *COL2A1* mutations with analysis of genotype-phenotype correlation in patients with a lethal type II collagen disorder *G R Mortier, M Weis, L Nuytinck, L M King, D J Wilkin, A De Paepe, R S Lachman, D L Rimoin, D R Eyre, D H Cohn*
272 Universal primer quantitative fluorescent multiplex (UPQFM) PCR: a method to detect major and minor rearrangements of the low density lipoprotein receptor gene *K E Heath, I N M Day, S E Humphries*
281 Parental origin and mechanisms of formation of cytogenetically recognisable de novo direct and inverted duplications *D Kotzot, M-J Martinez, G Bagci, S Basaran, A Baumer, F Binkert, L Brecevic, C Castellan, K Chrzanowska, F Dutly, A Gutkowska, S B Karaüzüm, M Krajewska-Walasek, G Luleci, P Miny, M Riegel, S Schuffenhauer, H Seidel, A Schinzel*
287 An unbalanced submicroscopic translocation t(8;16)(q24.3;p13.3)pat associated with tuberous sclerosis complex, adult polycystic kidney disease, and hypomelanosis of Ito *B H J Eussen, G Bartalini, L Bakker, P Balestri, C Di Lucca, J O Van Hemel, H Dauwerse, A M W van den Ouweland, C Ris-Stalpers, S Verhoef, D J J Halley, A Fois*
292 Clinical and radiological assessment of a family with mild brachydactyly type A1: the usefulness of metacarpophalangeal profiles *C M Armour, D E Bulman, A G W Hunter*

Letters to the Editor
297 Can hair be used to screen for breast cancer? *A Howell, J G Grossmann, K C Cheung, L Kanbi, D G R Evans, S S Hasnain*
298 Mutation analysis of *SMAD2*, *SMAD3*, and *SMAD4* genes in hereditary non-polyposis colorectal cancer *S Roth, M Johansson, A Loukola, P Peltomäki, H Järvinen, J-P Mecklin, L A Aaltonen*
301 Novel mutation in the *MYOC* gene in primary open angle glaucoma patients *J P C Vasconcellos, M B Melo, V P Costa, D M L Tsukumo, D S Bassáres, S Bordin, S T O Saad, F F Costa*
303 Three novel *SALL1* mutations extend the mutational spectrum in Townes-Brocks syndrome *C Blanck, J Kohlhase, S Engels, P Burfeind, W Engel, A Bottani, M S Patel, H Y Kroes, J M Cobben*
307 Genotype-phenotype correlation in three homozygotes and nine compound heterozygotes for the cystic fibrosis mutation 2183AA→G shows a severe phenotype *M O Kilinç, V N Ninis, A Tolun, X Estivill, T Casals, A Savov, E Dagli, F Karakoç, M Demirkol, G Hüner, F Özkinay, E Demir, J L Seculi, J Pena, C Bousono, J Ferrer-Calvete, C Calvo, G Glover, I Kremenski*
309 Alkaptonuria in Italy: polymorphic haplotype background, mutational profile, and description of four novel mutations in the homogentisate 1,2-dioxygenase gene *B Porfirio, I Chiarelli, C Graziano, A Mannoni, A Morrone, E Zammarchi, D Beltrán-Valero de Bernabé, S R de Córdoba*
312 Rough skin, brittle hair, and photosensitivity: a mild phenotypic variant of trichothiodystrophy *R Savarirayan, R J M Gardner, R D Sinclair, M McDowell, J E Cleaver*
314 The first description of lethal pterygium syndrome with facial clefting (Bartsocas-Papas syndrome) in 1600 *P D Turnpenny, R Hole*
315 Sex reversal and diaphragmatic hernia in phenotypically female sibs with normal XY chromosomes *S Manouvrier-Hanu, R Besson, L Cousin, C Jeanpierre, N Kacet, M Cartigny, L Devisme, L Storme, B de Martinville, P Lequien*
318 Clinical variability of Stickler syndrome with a *COL2A1* haploinsufficiency mutation: implications for genetic counselling *J Faber, A Winterpacht, B Zabel, W Gnoinski, A Schinzel, B Steinmann, A Superti-Furga*

No 5 MAY 2000

Page **Review article**
321 The Smith-Lemli-Opitz syndrome *R I Kelley, R C M Hennekam*

Original articles
336 Novel germline mutations in the *PTEN* tumour suppressor gene found in women with multiple cancers *I De Vivo, D M Gertig, S Nagase, S E Hankinson, R O'Brien, F E Speizer, R Parsons, D J Hunter*
342 Chromosome 8p alterations in sporadic and *BRCA2* 999del5 linked breast cancer *B I Sigbjörnsdottir, G Ragnarsson, B A Agnarsson, C Huiping, R B Barkardottir, V Egilsson, S Ingvarsson*
348 Familial clear cell renal cell carcinoma (FCRC): clinical features and mutation analysis of the *VHL*, *MET*, and *CUL2* candidate genes *E R Woodward, S C Clifford, D Astuti, N A Affara, E R Maher*
354 Efficacy of a touchscreen computer based family cancer history questionnaire and subsequent cancer risk assessment *J Westman, H Hampel, T Bradley*
361 A cross section of autosomal recessive limb-girdle muscular dystrophies in 38 families *P Dinçer, Z Akçören, E Demir, I Richard, Ö Sancak, G Kale, Ş Özme, A Karaduman, E Tan, J A Urtizberea, J S Beckmann, H Topaloglu*

Short reports

368 A novel C202F mutation in the connexin26 gene (*GJB2*) associated with autosomal dominant isolated hearing loss *L Morlé, M Bozon, N Alloisio, P Latour, A Vandenberghe, H Plauchu, L Collet, P Edery, J Godet, G Lina-Granade*

371 Glycine to tryptophan substitution in type I collagen in a patient with OI type III: a unique collagen mutation *L Nuytinck, T Tükel, H Kayserili, M Y Apak, A De Paepe*

Letters to the Editor

376 Phosphorylase kinase deficient liver glycogenosis: progression to cirrhosis in infancy associated with *PHKG2* mutations (H144Y and L225R) *B Burwinkel, M S Tanner, M W Kilimann*

377 Familial Wilms tumour resulting from *WT1* mutation: intronic polymorphism causing artefactual constitutional homozygosity *K Pritchard-Jones, N Rahman, M Gerrard, D Variend, L King-Underwood*

380 Silver-Russell syndrome and ring chromosome 7 *E L Wakeling, M Hitchins, P Stanier, D Monk, G E Moore, M A Preece*

380 Variants of *STAT6* (signal transducer and activator of transcription 6) in atopic asthma *P-S Gao, X-Q Mao, M H Roberts, Y Arinobu, M Akaiwa, T Enomoto, Y Dake, M Kawai, S Sasaki, N Hamasaki, K Izuhara, T Shirakawa, J M Hopkin*

382 No linkage or association of the *IL-4Rα* gene Q576R mutation with atopic asthma in Italian families *C Patuzzo, E Trabetti, G Malerba, L C Martinati, A L Boner, L Pescollderungg, G Zanoni, P F Pignatti*

384 Importance of the autosomal recessive retinitis pigmentosa locus on 1q31-q32.1 (RP12) and mutation analysis of the candidate gene *RGS16* (*RGS-r*) *D A R Bessant, A M Payne, B E Snow, G Antiñolo, S Q Mehdi, A C Bird, D P Siderovski, S S Bhattacharya*

387 Incidence and molecular mechanism of aberrant splicing owing to a G→C splice acceptor site mutation causing Smith-Lemli-Opitz syndrome *H R Waterham, W Oostheim, G J Romeijn, R J A Wanders, R C M Hennekam*

389 Clinical and molecular cytogenetic studies of a large de novo interstitial deletion 16q11.2-16q21 including the putative transcription factor gene *SALL1* *H Knoblauch, G Thiel, S Tinschert, H Körner, C Tennstedt, R Chaoui, J Kohlhase, C Dixkens, C Blanck*

392 Oculocutaneous albinism type 2 with a *P* gene missense mutation in a patient with Angelman syndrome *S Saitoh, N Oiso, T Wada, O Narazaki, K Fukai*

394 Anticipation in progressive diaphyseal dysplasia *J M Saraiva*

396 Hereditary neuropathy with liability to pressure palsies: two cases with a reciprocal translocation t(16;17)(q12;p11.2) interrupting the *PMP22* gene *M Nadal, A Valiente, A Domènech, M Pritchard, X Estivill, M A Ramos-Arroyo*

399 **Book reviews**

399 **Notices**

399 **Corrections**

400 **Notice for contributors**

Electronic letters

e1 Detection of fetal cells in transcervical samples using X22 marker *M Adinolfi, V Cirigliano*

e2 Autosomal translocation associated with premature ovarian failure *K A Burton, C C Van Ee, K Purcell, I Winship, A N Shelling*

e3 Genotype-phenotype correlations in tuberous sclerosis *P J De Vries, P F Bolton*

No 6 JUNE 2000

Page

Review article

401 Perfect endings: a review of subtelomeric probes and their use in clinical diagnosis *S J L Knight, J Flint*

Original articles

410 Over-representation of *PPARγ* sequence variants in sporadic cases of glioblastoma multiforme: preliminary evidence for common low penetrance modifiers for brain tumour risk in the general population *X-P Zhou, W M Smith, O Gimm, E Mueller, X Gao, P Sarraf, T W Prior, C Plass, A von Deimling, P McL Black, A J Yates, C Eng*

415 FRAXA and FRAXE: the results of a five year survey *S A Youings, A Murray, N Dennis, S Ennis, C Lewis, N McKechnie, M Pound, A Sharrock, P Jacobs*

422 Molecular characterisation of congenital glaucoma in a consanguineous Canadian community: a step towards preventing glaucoma related blindness *S N Martin, J Sutherland, A V Levin, R Klose, M Priston, E Héon*

428 Circadian rhythm abnormalities of melatonin in Smith-Magenis syndrome *L Potocki, D Glaze, D-X Tan, S-S Park, C D Kashork, L G Shaffer, R J Reiter, J R Lupski*

434 Five cases of isolated glycerol kinase deficiency, including two families: failure to find genotype:phenotype correlation *C A Sargent, A Kidd, S Moore, J Dean, G T N Besley, N A Affara*

Short reports

442 Delineation of a complex karyotypic rearrangement by microdissection and CGH in a family affected with split foot *J Weimer, M Kiechle, U Wiedemann, H Tönnies, H Neitzel, E Ruhenstroth, A Ovens-Raeder, N Arnold*

446 Tietz syndrome (hypopigmentation/deafness) caused by mutation of *MITF* *S D Smith, P M Kelley, J B Kenyon, D Hoover*

Letters to the Editor

449 Fine molecular mapping of the 4p16.3 aneuploidy syndromes in four translocation families *K Fagan, V Soubjaki, P Donald, G Turner, M Partington*

452 Investigation of meiotic rearrangements in DGS/VCFS patients with a microdeletion 22q11.2 *D Trost, W Wiebe, S Uhlhaas, P Schwindt, G Schwanitz*

454 Pure trisomy 20p resulting from isochromosome formation and whole arm translocation *R U Sidwell, M Pinson, B Gibbons, S Byatt, E C Svennevik, R J Hastings, D M Flynn*

458 A *SALL1* mutation causes a branchio-oto-renal syndrome-like phenotype *S Engels, J Kohlhase, J McGaughran*

460 New MR/MCA syndrome with distinct facial appearance and general habitus, broad and webbed neck, hypoplastic inverted nipples, epilepsy, and pachygyria of the frontal lobes *J-P Fryns, S Aftimos*

463 The mitochondrial genome in Wolfram syndrome *T G Barrett, M Scott-Brown, A Seller, A Bednarz, K Poulton, J Poulton*
466 Two further cases of Sener syndrome: frontonasal dysplasia and dilated Virchow-Robin spaces *S A Lynch, K Hall, S Precious, A O M Wilkie, J A Hurst*
470 The psychological impact of a cancer family history questionnaire completed in general practice *V Leggatt, J Mackay, T M Marteau, J R W Yates*
472 Attitudes to genetic testing for breast cancer susceptibility in women at increased risk of developing hereditary breast cancer *B Meiser, P Butow, A Barratt, G Suthers, M Smith, A Colley, E Thompson, K Tucker*
476 Attitudes of von Hippel-Lindau disease patients towards presymptomatic genetic diagnosis in children and prenatal diagnosis *M Levy, S Richard, on behalf of the French VHL Study Group*
479 **Correction**
480 **Notice**

Electronic letters

e4 Rapid detection of mirodeletions using fluorescence in situ hybridisation (FISH) on buccal smears *A W M Nieuwint, J M Van Hagen, Y M Heins, K Madan, L P Ten Kate*
e5 Mutation analysis of *GABRR1* and *GABRR2* in autosomal recessive retinitis pigmentosa *(RP25) I Marcos, A Ruiz, C J Blaschak, S Borrego, G R Cutting, G Antiñolo*

No 7 JULY 2000

Page **Review article**
481 The genetics of childhood cataract *P J Francis, V Berry, S S Bhattacharya, A T Moore*

Original articles

489 A clinical study of 57 children with fetal anticonvulsant syndromes *S J Moore, P Turnpenny, A Quinn, S Glover, D J Lloyd, T Montgomery, J C S Dean*
498 The *ACE* I allele is associated with increased risk for ruptured intracranial aneurysms *M Keramatipour, R S McConnell, P Kirkpatrick, S Tebbs, R A Furlong, D C Rubinsztein*
501 Gene amplification in PNETs/medulloblastomas: mapping of a novel amplified gene within the *MYCN* amplicon *M C Frühwald, M S O'Dorisio, L J Rush, J L Reiter, D J Smiraglia, G Wenger, J F Costello, P S White, R Krahe, G M Brodeur, C Plass*
510 Complementation studies in the *cblA* class of inborn error of cobalamin metabolism: evidence for interallelic complementation and for a new complementation class (*cblH*) *D Watkins, N Matiaszuk, D S Rosenblatt*
514 Predominance of a 6 bp deletion in exon 2 of the LDL receptor gene in Africans with familial hypercholesterolaemia *R Thiart, C L Scholtz, J Vergotine, C F Hoogendijk, J N P de Villiers, H Nissen, K Brusgaard, D Gaffney, M S Hoffs, W J H Vermaak, M J Kotze*

Short reports

520 Genitopatellar syndrome: a new condition comprising absent patellae, scrotal hypoplasia, renal anomalies, facial dysmorphism, and mental retardation *V Cormier-Daire, M Chauvet, S Lyonnet, M Briard, A Munnich, M Le Merrer*
525 Maternal uniparental heterodisomy of chromosome 14: chromosomal mechanism and clinical follow up *D Sanlaville, M C Aubry, Y Dumez, M C Nolen, J Amiel, M P Pinson, S Lyonnet, A Munnich, M Vekemans, N Morichon-Delvallez*
529 Molecular cytogenetic characterisation of partial trisomy 9q in a case with pyloric stenosis and a review *A Heller, J Seidel, A Hübler, H Starke, V Beensen, G Senger, M Rocchi, J Wirth, I Chudoba, U Claussen, T Liehr*

Letters to the Editor

533 Incidence of germline *HMLH1* and *HMSH2* mutations (HNPCC patients) among newly diagnosed colorectal cancers in a Slovenian population *M Ravnik-Glavač, U Potočnik, D Glavač*
536 Does the survival motor neuron protein (SMN) interact with Bcl-2? *D D Coovert, T T Le, G E Morris, N T Man, M Kralewski, M Sendtner, A H M Burghes*
539 Novel mutations in the homogentisate-1,2-dioxygenase gene identified in Slovak patients with alkaptonuria *A Zatková, H Poláková, L Micutková, M Zvarik, V Bošák, E Feráková, J Matušek, V Ferák, L Kádasi*
542 Clinical and molecular correlates of somatic mosaicism in neurofibromatosis 2 *M E Baser, A J Wallace, T Strachan, D G R Evans*
543 Many ΔF508 heterozygote neonates with transient hypertrypsinaemia have a second, mild *CFTR* mutation *J Boyne, S Evans, R J Pollitt, C J Taylor, A Dalton*
547 Further evidence for genetic heterogeneity of autosomal dominant disorders with accumulation of multiple deletions of mitochondrial DNA *G van Goethem, A Löfgren, J-J Martin, C van Broeckhoven*
548 Liebenberg syndrome: brachydactyly with joint dysplasia (MIM 186550): a second family *G Tiberio, M C Digilio, M Graziani, F Testa, A Giannotti*
551 Prenatal detection of trisomy for the entire long arm of chromosome 7 *B V Ndah, J A Stead, L R Brancazio, M Hummel, S L Wenger*
553 Cockayne syndrome associated with low CSF 5-hydroxyindole acetic acid levels *C J Ellaway, A Duggins, V S Fung, J W Earl, R Kamath, P G Parsons, J A Antony, K N North*
557 Unilateral lobar pulmonary agenesis in sibs *S Fokstuen, A Schinzel*
559 **Correction**
560 **Instructions for authors**

Electronic letters

e6 Two novel germline mutations of the retinoblastoma gene (*RB1*) that show incomplete penetrance, one splice site and one missense *H Scheffer, P Van der Vlies, M Burton, E Verlind, A C Moll, S M Imhof, C H C M Buys*
e7 Mutational germline analysis of *hMSH2* and *hMLH1* genes in early onset colorectal cancer patients *M Montera, N Resta, C Simone, G Guanti, C Marchese, S Civitelli, A Mancini, S Pozzi, L De Salvo, D Bruzzone, A Donadini, L Romio, C Mareni*
e8 Alström syndrome: confirmation of linkage to chromosome 2p12-13 and phenotypic heterogeneity in three affected sibs *U Zumsteg, P Y Muller, A R Miserez*

e9 Evaluation of the *HOX11L1* gene as a candidate for congenital disorders of intestinal innervation *M Costa, M Fava, M Seri, R Cusano, M Sancandi, P Forabosco, M Lerone, G Martucciello, G Romeo, I Ceccherini*

No 8 AUGUST 2000

Page **Review article**

561 Autosomal dominant sacral agenesis: Currarino syndrome *S A Lynch, Y Wang, T Strachan, J Burn, S Lindsay*

Original articles

567 Ten years of presymptomatic testing for Huntington's disease: the experience of the UK Huntington's Disease Prediction Consortium *P S Harper, C Lim, D Craufurd, on behalf of the UK Huntington's Disease Prediction Consortium*

572 *RET* genotypes comprising specific haplotypes of polymorphic variants predispose to isolated Hirschsprung disease *S Borrego, A Ruiz, M E Saez, O Gimm, X Gao, M Lòpez-Alonso, A Hernández, F A Wright, G Antiñolo, C Eng*

579 Identification of four novel *PMM2* mutations in congenital disorders of glycosylation (CDG) Ia French patients *S Vuillaumier-Barrot, G Hetet, A Barnier, T Dupré, M Cuer, P de Lonlay, V Cormier-Daire, G Durand, B Grandchamp, N Seta*

581 Detailed mapping of a congenital heart disease gene in chromosome 3p25 *E K Green, M D Priestley, J Waters, C Maliszewska, F Latif, E R Maher*

588 The role of hypermethylation of the *hMLH1* promoter region in HNPCC versus MSI+ sporadic colorectal cancers *J M D Wheeler, A Loukola, L A Aaltonen, N J McC Mortensen, W F Bodmer*

593 FISH deletion mapping defines a single location for the Y chromosome stature gene, *GCY* *S Kirsch, B Weiss, M De Rosa, T Ogata, G Lombardi, G A Rappold*

Short reports

600 Interstitial deletion in Xp22.3 is associated with X linked ichthyosis, mental retardation, and epilepsy *B C Gohlke, K Haug, M Fukami, W Friedl, M Nocker, G A Rappold, F Haverkamp*

603 Twin sisters, monozygotic with the fragile X mutation, but with a different phenotype *R Willemsen, R Olmer, Y De Diego Otero, B A Oostra*

Clinical genetics in practice

605 A survey of the current clinical facilities for the management of familial cancer in Europe *S V Hodgson, N E Haites, with BIOMED II partners M Caligo, J Chang-Claude, D Eccles, G Evans, P Møller, P Morrison, C M Steel, D Stoppa-Lyonnet, H Vasen*

Letters to the Editor

608 Mutation analysis of the methyl-CpG binding protein 2 gene (*MECP2*) in patients with Rett syndrome *K Obata, T Matsuishi, Y Yamashita, T Fukuda, K Kuwajima, I Horiuchi, S Nagamitsu, R Iwanaga, A Kimura, I Omori, S Endo, K Mori, I Kondo*

610 Mutations in the *MECP2* gene in a cohort of girls with Rett syndrome *K Hampson, C G Woods, F Latif, T Webb*

612 Monosomy and trisomy 1q44-qter in two sisters originating from a half cryptic 1q;15p translocation *N Villa, E Sala, D Colombo, M Dell'Orto, D Grioni, L Dalprà*

615 A constitutional homozygous mutation in the *RB1* gene in a patient with unilateral retinoblastoma *F Sánchez, E Mateu, M Beneyto, C Nájera, F Prieto*

620 The gene for branchio-oculo-facial syndrome does not colocalise to the *EYA1-4* genes *L S Correa-Cerro, I Kennerknecht, W Just, W Vogel, D Müller*

623 Importance of clinical evaluation and molecular testing in the branchio-oto-renal (BOR) syndrome and overlapping phenotypes *S Rickard, M Boxer, R Trompeter, M Bitner-Glindzicz*

627 Equal expression of type X collagen mRNA from mutant and wild type *COL10A1* alleles in growth plate cartilage from a patient with metaphyseal chondrodysplasia type Schmid *C A Gregory, B Zabel, M E Grant, R P Boot-Handford, G A Wallis*

629 The relationship between neonatal immunoreactive trypsinogen, ΔF508, and IVS8-5T *J Massie, D Du Sart, K Forshaw, J Carlin, S M Forrest*

632 Epidemiology of neurofibromatosis type 1 (NF1) in northern Finland *M Poyhonen, S Kytölä, J Leisti*

636 Genetic registers in clinical practice: a survey of UK clinical geneticists *J C S Dean, D R Fitzpatrick, P A Farndon, H Kingston, D Cusine*

Electronic letters

e10 Duplication of medial 15q confirmed by FISH *C E Browne, E Hatchwell, A Protopapos, J Ramos*

e11 A child with bisatellited, dicentric chromosome 15 arising from a maternal paracentric inversion of chromosome 15q *M L Whiteford, C Baird, S Kinmond, B Donaldson, H R Davidson*

e12 A family with hereditary port wine stain *J N Berg, A A Quaba, A Georgantopoulou, M E M Porteous*

e13 Absence of germline $p16^{INK4a}$ alterations in *p53* wild type Li-Fraumeni syndrome families *C Portwine, J Lees, S Verselis, F P Li, D Malkin*

e14 Distal spinal muscular atrophy with vocal cord paralysis (dSMA-VII) is not linked to the *MPD2* locus on chromosome 5q31 *M McEntagart, G Spurlock, C Jackson, P Harper, N Rahman*

e15 Fetal bowel hyperechogenicity may indicate mild atypical cystic fibrosis: a case associated with a complex *CFTR* allele *M J Abramowicz, B Dessars, C Sevens, M Goossens, E G Boulandet*

e16 Distribution of *CFTR* gene mutations in cystic fibrosis patients from Estonia *M Teder, T Klaassen, E Oitmaa, K Kaasik, A Metspalu*

No 9 SEPTEMBER 2000

Page **Original articles**

641 Sensitivity and specificity of clinical criteria for hereditary non-polyposis colorectal cancer associated mutations in *MSH2* and *MLH1* *S Syngal, E A Fox, C Eng, R D Kolodner, J E Garber*

646 Recurrent germline mutation in *MSH2* arises frequently de novo *D C Desai, J C Lockman, R B Chadwick, X Gao, A Percesepe, D G R Evans, M Miyaki, S T Yuen, P Radice, E R Maher, F A Wright, A de la Chapelle*

653 Identification of *PTEN* mutations in metastatic melanoma specimens *J T Çelebi, I Shendrik, D N Silvers, M Peacocke*

658 *JAGGED*1 expression in human embryos: correlation with the Alagille syndrome phenotype *E A Jones, M Clement-Jones, D I Wilson*

663 A new X linked mental retardation (XLMR) syndrome with short stature, small testes, muscle wasting, and tremor localises to Xq24-q25 *D A Cabezas, R Slaugh, F Abidi, J F Arena, R E Stevenson, C E Schwartz, H A Lubs*

669 A novel mutation in the thiamine responsive megaloblastic anaemia gene *SLC19A2* in a patient with deficiency of respiratory chain complex *I C Scharfe, M Hauschild, T Klopstock, A J M Janssen, P H Heidemann, T Meitinger, M Jaksch*

674 Characterisation of the human *GFRα-3* locus and investigation of the gene in Hirschsprung disease *C I Onochie, L M Korngut, J B Vanhorne, S M Myers, D Michaud, L M Mulligan*

680 Genetics of club foot in Maori and Pacific people *C Chapman, N S Stott, R V Port, R O Nicol*

Clinical genetics in practice

684 Evidence based medicine in practice: lessons from a Scottish clinical genetics project *H Campbell, N Bradshaw, R Davidson, J Dean, D Goudie, S Holloway, M Porteous*

Short reports

692 A novel mutation in the mitochondrial $tRNA^{Ser(UCN)}$ gene in a family with non-syndromic sensorineural hearing impairment *T P Hutchin, M J Parker, I D Young, A C Davis, L J Pulleyn, J Deeble, N J Lench, A F Markham, R F Mueller*

695 The *ACE* gene and Alzheimer's disease susceptibility *Y Narain, A Yip, T Murphy, C Brayne, D Easton, J G Evans, J Xuereb, N Cairns, M M Esiri, R A Furlong, D C Rubinsztein*

Letters to the Editor

698 Constitutional *WT1* mutations correlate with clinical features in children with progressive nephropathy *A Takata, H Kikuchi, R Fukuzawa, S Ito, M Honda, J-I Hata*

701 Interstitial deletion of chromosome 17 (del(17)(q22q23.3)) confirms a link with oesophageal atresia *A J Marsh, D Wellesley, D Burge, M Ashton, C E Browne, N R Dennis, I K Temple*

704 Mutational analysis of Sanfilippo syndrome type A (MPS IIIA): identification of 13 novel mutations *C E Beesley, E P Young, A Vellodi, B G Winchester*

707 Genotype-phenotype relationship of Niemann-Pick disease type C: a possible correlation between clinical onset and levels of NPC1 protein in isolated skin fibroblasts *T Yamamoto, H Ninomiya, M Matsumoto, Y Ohta, E Nanba, Y Tsutsumi, K Yamakawa, G Millat, M T Vanier, P G Pentchev, K Ohno*

712 Crigler-Najjar syndrome type II resulting from three different mutations in the bilirubin uridine 5'-diphosphate-glucuronosyltransferase (*UGT1A1*) gene *A Iolascon, A Meloni, B Coppola, M C Rosatelli*

713 I705 variant in the low density lipoprotein receptor gene has no effect on plasma cholesterol levels *K E Heath, R A Whittall, G J Miller, S E Humphries*

715 Absence of germline mutations in *MINPPI*, a phosphatase encoding gene centromeric of *PTEN*, in patients with Cowden and Bannayan-Riley-Ruvalcaba syndrome without germline *PTEN* mutations *P M Dahia, O Gimm, H Chi, D J Marsh, P R Reynolds, C Eng*

717 Mosaicism in Alport syndrome and genetic counselling *M Bruttini, F Vitelli, I Meloni, G Rizzari, M D Volpe, G Mazzucco, M de Marchi, A Renieri*

719 Breast hypoplasia and disproportionate short stature in the ear, patella, short stature syndrome: expansion of the phenotype? *P A Terhal, M G E M Ausems, Y van Bever, L P ten Kate, P F Dijkstra, G M C Kuijpers*

721 Pili torti et canaliculi and agenesis of the teeth: report of a new "pure" hair-tooth ectodermal dysplasia in a Norwegian family *E Selvaag*

723 Skin pigmentary anomalies in a mosaic form of partial tetrasomy 3q *P M Kroisel, E Petek, K Wagner*

725 Reduction of the genetic interval for lymphoedema-distichiasis to below 2 Mb *R Bell, G Brice, A H Child, V A Murday, S Mansour, C J Sandy, J R O Collin, P Mortimer, D F Callen, K Burnand, S Jeffery*

727 **Book review**

728 **Instructions for authors**

Electronic letters

e17 *BRCA2* germline mutations among early onset breast cancer patients unselected for family history of the disease *J Plaschke, T Commer, C Jacobi, H K Schackert, J Chang-Claude*

e18 Cytosine methylation confers instability on the cardiac troponin T gene in hypertrophic cardiomyopathy *L G D'Cruz, C Baboonian, H E Phillimore, R Taylor, P M Elliott, A Varnava, F Davison, W J McKenna, N D Carter*

e19 Diagnosis of maternal uniparental disomy of chromosome 7 with a methylation specific PCR assay *K Kosaki, R Kosaki, W P Robinson, W J Craigen, L G Shaffer, S Sato, N Matsuo*

e20 Mapping of the human genes (*SLC23A2* and *SLC23A1*) coding for vitamin C transporters 1 and 2 (SVCT1 and SVCT2) to 5q23 and 20p12, respectively *C A Stratakis, S E Taymans, R Daruwala, J Song, M Levine*

e21 Deletion (2)(p14p15) in a child with severe neurodevelopmental delay *I M Amir, K I Al-Tawil, M M Al-Hathal*

e22 Partial trisomy 22 in a liveborn resulting from a rearrangement between chromosomes 6 and 22 *G Mirza, K Imaizumi, J Ragoussis*

e23 DiGeorge syndrome with discordant phenotype in monozygotic twins *G Hillebrand, R Siebert, E Simeoni, R Santer*

e24 Proximal 10q trisomy: a new case with anal atresia *F W F Lam, W K Chan, S T S Lam, W P Chu, N S Kwong*

e25 Achondroplasia and nail-patella syndrome: the compound phenotype *M J Wright, M C Ain, M V Clough, G A Bellus, O Hurko, I Mcintosh*

Review article

729 Channelopathies: ion channel defects linked to heritable clinical disorders *R Felix*

Original articles

741 Sporadic primary pulmonary hypertension is associated with germline mutations of the gene encoding BMPR-II, a receptor member of the TGF-β family *J R Thomson, R D Machado, M W Pauciulo, N V Morgan, M Humbert, G C Elliott, K Ward, M Yacoub, G Mikhail, P Rogers, J Newman, L Wheeler, T Higenbottam, J S R Gibbs, J Egan, A Crozier, A Peacock, R Allcock, P Corris, J E Loyd, R C Trembath, W C Nichols*

746 *ATR-X* mutations cause impaired nuclear location and altered DNA binding properties of the XNP/ATR-X protein *C Cardoso, Y Lutz, C Mignon, E Compe, D Depetris, M-G Mattei, M Fontes, L Colleaux*

752 Divergent outcomes of intrachromosomal recombination on the human Y chromosome: male infertility and recurrent polymorphism *P Blanco, M Shlumukova, C A Sargent, M A Jobling, N Affara, M E Hurles*

759 Mutation analysis of the spastin gene (*SPG4*) in patients with hereditary spastic paraparesis *J C Lindsey, M E Lusher, C J McDermott, K D White, E Reid, D C Rubinsztein, R Bashir, J Hazan, P J Shaw, K M D Bushby*

766 Dipeptidyl carboxypeptidase 1 (*DCP1*) and butyrylcholinesterase (*BCHE*) gene interactions with the apolipoprotein E ε4 allele as risk factors in Alzheimer's disease and in Parkinson's disease with coexisting Alzheimer pathology *K M Mattila, J O Rinne, M Röyttä, P Laippala, T Pietilä, H Kalimo, T Koivula, H Frey, T Lehtimäki*

771 Two translocations of chromosome 15q associated with dyslexia *J Nopola-Hemmi, M Taipale, T Haltia, A Lehesjoki, A Voutilainen, J Kere*

Hypothesis

776 Two common forms of the human *MLH1* gene may be associated with functional differences *P Hutter, A Couturier, C Rey-Berthod*

Short report

782 *FMR3* is a novel gene associated with *FRAXE* CpG island and transcriptionally silent in *FRAXE* full mutations *J Gécz*

Letters to the Editor

785 The mutation spectrum in Holt-Oram syndrome *S J Cross, Y-H Ching, Q Y Li, L Armstrong-Buisseret, S Spranger, S Lyonnet, D Bonnet, M Penttinen, P Jonveaux, B Leheup, G Mortier, C van Ravenswaaij, C-A Gardiner, J D Brook, R Newbury-Ecob*

787 Hemiplegic cerebral palsy and the factor V Leiden mutation *J L Halliday, D Reddihough, K Byron, H Ekert, M Ditchfield*

789 Analysis of the human tumour necrosis factor-alpha (TNFα) gene promoter polymorphisms in children with bone cancer *A Patiño-García, E Sotillo-Piñeiro, C Modesto, L Sierrasesúmaga*

792 Low prevalence of germline *BRCA1* mutations in early onset breast cancer without a family history *D Ellis, J Greenman, S Hodgson, S McCall, F Lalloo, J Cameron, L Izatt, G Scott, C Jacobs, S Watts, W Chorley, C Perrett, K MacDermot, S Mohammed, G Evans, C G Mathew*

794 Delineation of a new syndrome: clustering of pyloric stenosis, endometriosis, and breast cancer in two families *A Liede, T Pal, M Mitchell, S A Narod*

796 Punctate calcification of the epiphyses, visceral malformations, and craniofacial dysmorphism in a female baby *A Slavotinek, H Kingston*

798 Unexpected high frequency of de novo unbalanced translocations in patients with Wolf-Hirschhorn syndrome (WHS) *D Wieczorek, M Krause, F Majewski, B Albrecht, P Meinecke, O Riess, G Gillessen-Kaesbach*

804 Mosaicism for a dup(12)(q22q13) in a patient with hypomelanosis of Ito and asymmetry *H Schmidt, S Uhrig, G Lederer, J Murken, M R Speicher, S Schuffenhauer*

807 An analphoid supernumerary marker chromosome derived from chromosome 3 ascertained in a fetus with multiple malformations *A E Cockwell, B Gibbons, I E Moore, J A Crolla*

810 Why patients do not attend for their appointments at a genetics clinic *L Humphreys, A G W Hunter, A Zimak, A O'Brien, Y Korneluk, M Cappelli*

815 **Correction**

816 **Instructions for authors**

Electronic letters

e26 Genetics and deafness: what do families want? *M J Parker, H M Fortnum, I D Young, A C Davis*

e27 A case of dyschondrosteosis from Roman Britain *H A Waldron*

e28 Xp;Yp translocation inherited from the father in an *SRY*, *RBM*, and *TSPY* positive true hermaphrodite with oligozoospermia *L Jakubowski, A Jeziorowska, M Constantinou, Z Helszer, A Baumstark, W Vogel, D Mikiewicz-Sygula, B Kaulzewski*

e29 MPS II in females: molecular basis of two different cases *S Cudry, I Tigaud, R Froissart, V Bonnet, I Maire, D Bozon*

e30 Partial tetrasomy 21 in a male infant *A M Slavotinek, X-N Chen, A Jackson, L Gaunt, A Campbell, J Clayton-Smith, J R Korenberg*

e31 Benign familial infantile convulsions: report of a UK family and confirmation of genetic heterogeneity *D Baralle, A M Dearlove, R Beach, C Ffrench-Constant, E Reid*

e32 Low frequency of microsatellite instability in *BRCA1* mutated breast tumours *C Vaurs-Barrière, F R Penault-Llorca, V Laplace-Marieze, N Presneau, C M Maugard, M Fiche, A Hardouin, Y-J Bignon*

No 11 NOVEMBER 2000 Page

Review article

817 Multiple endocrine neoplasia type 2 and *RET*: from neoplasia to neurogenesis *J R Hansford, L M Mulligan*

Commentary

828 Will the real Cowden syndrome please stand up: revised diagnostic criteria *C Eng*

Original articles

831 A novel genetic locus for low renin hypertension: familial hyperaldosteronism type II maps to chromosome 7 (7p22) *A R Lafferty, D J Torpy, M Stowasser, S E Taymans, J P Lin, P Huggard, R D Gordon, C A Stratakis*

836 Characterisation and genetic mapping of a new X linked deafness syndrome *D M Martin, F J Probst, S A Camper, E M Petty*

842 Increase of FMRP expression, raised levels of *FMR1* mRNA, and clonal selection in proliferating cells with unmethylated fragile X repeat expansions: a clue to the sex bias in the transmission of full mutations? *U Salat, B Bardoni, D Wöhrle, P Steinbach*

851 Desmin splice variants causing cardiac and skeletal myopathy *K-Y Park, M C Dalakas, H H Goebel, V J Ferrans, C Semino-Mora, S Litvak, K Takeda, L G Goldfarb*

858 Disease associated balanced chromosome rearrangements: a resource for large scale genotype-phenotype delineation in man *M Bugge, G Bruun-Petersen, K Brøndum-Nielsen, U Friedrich, J Hansen, G Jensen, P K A Jensen, U Kristoffersson, C Lundsteen, E Niebuhr, K R Rasmussen, K Rasmussen, N Tommerup*

866 An evaluation of needs of female *BRCA1* and *BRCA2* carriers undergoing genetic counselling *K A Metcalfe, A Liede, E Hoodfar, A Scott, W D Foulkes, S A Narod*

Letters to the Editor

875 Congenital disorders of glycosylation IIa cause growth retardation, mental retardation, and facial dysmorphism *V Cormier-Daire, J Amiel, S Vuillaumier-Barrot, J Tan, G Durand, A Munnich, M Le Merrer, N Seta*

877 Characterisation of six large deletions in *TSC2* identified using long range PCR suggests diverse mechanisms including Alu mediated recombination *S L Dabora, A A Nieto, D Franz, S Jozwiak, A van Den Ouweland, D J Kwiatkowski*

883 Attitudes towards termination of pregnancy in subjects who underwent presymptomatic testing for the *BRCA1/BRCA2* gene mutation in The Netherlands *L N Lodder, P G Frets, R W Trijsburg, E J Meijers-Heijboer, J G M Klijn, M F Niermeijer*

884 Detailed mapping, mutation analysis, and intragenic polymorphism identification in candidate Noonan syndrome genes *MYL2, DCN, EPS8*, and *RPL6* *A Ion, A H Crosby, H Kremer, N Kenmochi, M van Reen, C Fenske, I van der Burgt, H G Brunner, K Montgomery, R S Kucherlapati, M A Patton, D C Page, E Mariman, S Jeffery*

886 Hall-Riggs syndrome: a possible second affected family? *M Silengo, R Rigardetto*

889 Dysmorphic sibs trisomic for the region 6q22.1→6q23.3 *D L M Goh, A S C Tan, J Y C Chen, J A van den Berghe*

892 A de novo complex chromosomal rearrangement involving chromosomes 2, 3, and 10 associated with microcephaly and early onset spasticity *W Emberger, E Petek, B Plecko-Startinig, P M Kroisel, H Zierler, K Wagner*

896 **Correction**

Electronic letters

e33 Clinical phenotypes and molecular characterisation of three patients with Ehlers-Danlos syndrome type VII *A C Nicholls, J L Sher, M J Wright, C Oley, R F Mueller, F M Pope*

e34 Idiopathic multicentric osteolysis presents early and is not linked to chromosome 18q21.1 *T J L de Ravel, G Matthijs, M Holvoet, C Wouters, E Legius, J P Fryns*

e35 Germline mosaicism for a *GNAS1* mutation and Albright hereditary osteodystrophy *M A Aldred, R J Bagshaw, K MacDermot, D Casson, S H Murch, J A Walker-Smith, R C Trembath*

e36 A CGC>CAT gene conversion-like event resulting in the R122H mutation in the cationic trypsinogen gene and its implication in the genotyping of pancreatitis *J-M Chen, O Raguenes, C Ferec, P H Deprez, C Verellen-Dumoulin*

e37 Familial craniofacial fibrous dysplasia: absence of linkage to *GNAS1* and the gene for cherubism *J Mangion, S Edkins, A N Goss, M R Stratton, A M Flanagan*

e38 Identification of three novel frameshift mutations in patients with Friedreich's ataxia *M A Pook, S A H Al-Mahdawi, N H Thomas, R Appleton, A Norman, R Mountford, S Chamberlain*

e39 Determination of the frequency of connexin26 mutations in inherited sensorineural deafness and carrier rates in the Tunisian population using DGGE *S Masmoudi, A Elgaied-Boulila, I Kassab, S Ben Arab, S Blanchard, J-E Bouzouita, M Drira, A Kassab, S Hachicha, C Petit, H Ayadi*

e40 Cardiovascular fibrosis, hydrocephalus, ophthalmoplegia, and visceral involvement in an American child with Gaucher disease *D L Stone, N Tayebi, C Coble, E I Ginns, E Sidransky*

No 12 DECEMBER 2000

Page

Review article

897 Neurofibromatosis type 2 *D G R Evans, M Sainio, Michael E Baser*

905 Chromatin modification and disease *C A Johnson*

Original articles

916 The *ALX4* homeobox gene is mutated in patients with ossification defects of the skull (foramina parietalia permagna, OMIM 168500) *W Wuyts, E Cleiren, T Homfray, A Rasore-Quartino, F Vanhoenacker, W Van Hul*

921 Epigenotype-phenotype correlations in Beckwith-Wiedemann syndrome *J R Engel, A Smallwood, A Harper, M J Higgins, M Oshimura, W Reik, P N Schofield, E R Maher*

927 Identification of cathepsin C mutations in ethnically diverse Papillon-Lefèvre syndrome patients *P S Hart, Y Zhang, E Firatli, C Uygur, M Lotfazar, M D Michalec, J J Marks, X Lu, B J Coates, W K Seow, R Marshall, D Williams, J B Reed, J T Wright, T C Hart*

933 Growth in North American white children with neurofibromatosis 1 (NF1) *J Szudek, P Birch, J M Friedman, the National Neurofibromatosis Foundation International Database Participants*

939 Cryptic von Hippel-Lindau disease: germline mutations in patients with haemangioblastoma only *F J Hes, S McKee, M J B Taphoorn, P Rehal, R B van der Luijt, R McMahon, J J van der Smagt, D Dow, R A Zewald, J Whittaker, C J M Lips, F MacDonald, P L Pearson, E R Maher*

Letters to the Editor

944 Use of MRI and audiological tests in presymptomatic diagnosis of type 2 neurofibromatosis (NF2) *D G R Evans, V Newton, W Neary, M E Baser, A Wallace, R Macleod, J P R Jenkins, J Gillespie, R T Ramsden*

947 Suggestive evidence for a site specific prostate cancer gene on chromosome 1p36 *M Badzioch, R Eeles, G Leblanc, W D Foulkes, G Giles, S Edwards, D Goldgar, J L Hopper, D T Bishop, P Møller, K Heimdal, D Easton, J Simard*

949 Comorbidity of 5,10-methylenetetrahydrofolate reductase and methionine synthase gene polymorphisms and risk for neural tube defects *G L Johanning, T Tamura, K E Johnston, K D Wenstrom*

951 Expression of HCM causing mutations: lessons learnt from genotype-phenotype studies of the South African founder *MYH7* A797T mutation *J Moolman-Smook, W de Lange, V Corfield, P Brink*

956 Germline and somatic mosaicism in achondroplasia *S Henderson, D Sillence, J Loughlin, B Bennetts, B Sykes*

958 Achondroplasia with the *FGFR3* 1138g→a (G380R) mutation in two sibs sharing a 4p haplotype derived from their unaffected father *D Sobetzko, S Braga, A Rüdeberg, A Superti-Furga*

959 Homozygous deletion of *SHOX* in a mentally retarded male with Langer mesomelic dysplasia *S P Robertson, D J Shears, P Oei, R M Winter, P J Scambler, S Aftimos, R Savarirayan*

964 Tandem triplication of chromosome 13q14 with inverted interstitial segment in a 4 year old girl *L Brecevic, S Basaran, F Dutly, B Röthlisberger, A Schinzel*

967 The first three mosaic cri du chat syndrome patients with two rearranged cell lines *C Perfumo, P C Mainardi, A Cali, G Coucourde, F Zara, S Cavani, J Overhauser, F D Bricarelli, M Pierluigi*

972 Abnormal sex differentiation and multiple congenital abnormalities in a subject harbouring an apparently balanced (6;8) translocation *A Ion, H Copin, M Barnoux, C Ajzenberg, A Lesourd, O Cussenot, J Lubetzki, L Telvi*

974 Distal trisomy 2p and arachnodactyly *D J Stalker, S Vigneswaren, P M Sharples, P W Lunt*

Electronic letters

e41 Spectrum of mutations in the *MECP2* gene in patients with infantile autism and Rett syndrome *C-W Lam, W-L Yeung, C-H Ko, P M K Poon, S-F Tong, K-Y Chan, I F M Lo, L Y S Chan, J Hui, V Wong, C-P Pang, Y M D Lo, T-F Fok*

e42 2157delG: a frequent mutation in *BRCA2* missed by PTT *J F Davies, E K Redmond, M C Cox, F I Lalloo, R Elles, D G R Evans*

e43 A clinical assessment of neurofibromatosis type 1 (NF1) and segmental NF in northern Finland *M Poyhonen*

e44 Exclusion of a disease relevant role of *PAX4* in the aetiology of Silver-Russell syndrome: screening for mutations and determination of imprinting status *S Mergenthaler, K Eggermann, J Tomiuk, M B Ranke, H A Wollmann, T Eggermann*

e45 Recurrence risks in undiagnosed mental retardation *G Turner, M Partington*

e46 Bardet-Biedl and Cohen syndromes: differential diagnostic criteria *M Warburg, R Riise, P Beales, F Flinter*

e47 CHARGE association in a child with de novo chromosomal aberration 46,X,der(X)t(X;2)(p22.1;q33) detected by spectral karyotyping *D Lev, O Nakar, I Bar-Am, A Zudik, N Watemberg, S Finkelstien, N Katzin, T Lerman-Sagie*